HARNESSING SCIENCE TO SOLVE GLOBAL POVERTY AND HUNGER

Flexibility and Freedom of Action Are Essential for Rapid Progress

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Peter C. Doherty
Nobel Laureate for Medicine

1998 Sir John Crawford Memorial Lecture

Consultative Group on International Agricultural Research (CGIAR)

THE CGIAR

The Consultative Group on International Agricultural Research (CGIAR) mobilizes the best in agricultural science on behalf of the world's poor and hungry. Through its research, the CGIAR promotes sustainable agriculture for food security in developing countries.

The CGIAR supports a network of sixteen international agricultural research centers, which implement an agreed-upon agenda in partnership with national governmental and non-governmental organizations, universities, and private industry. The Food and Agriculture Organization (FAO) of the United Nations, the United Nations Development Programme (UNDP), the United Nations Environment Programme (UNEP), and the World Bank cosponsor the CGIAR.

For more than a quarter century, the CGIAR has brought together the world's leading scientists and agricultural researchers in a unique South-North commitment to reduce poverty and hunger in developing countries. This is important because 95 percent of the 90 million people born every year live in the poorest countries. Whether researching food crops, forestry, livestock, irrigation management, aquatic resources, or policy, the CGIAR focuses on productivity and natural resources management—which are emphasized in its services to agricultural research systems in developing countries. CGIAR activities have contributed to global food security, helping to keep the environment healthy and farming sustainable.

The fifty-eight members that support the CGIAR include developing and developed countries, economies in transition, private foundations, and international and regional organizations. Developing-country participation has doubled in recent years. All twenty-two members of the OECD (Organisation for Economic Co-operation and Development) Development Assistance Committee belong to the CGIAR. Ismail Serageldin, Vice President for Special Programs at the World Bank, serves as the CGIAR Chairman.

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CGIAR International Centers Week
October 29, 1998
Washington, DC

Published by the Consultative Group on International Agricultural Research, CGIAR Secretariat, 1818 H Street, NW, Washington, DC, 20433, United States of America

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Sir John Crawford (1910-1984) was a distinguished Australian civil servant, educator, and agriculturalist who was one of the founders of the Consultative Group on International Agricultural Research and the first Chair of the CGIAR's Technical Advisory Committee. The Sir John Crawford Memorial Lecture has been sponsored by the Australian Government since 1985 in his honor.

Sir John Crawford functioned at various stages of his career as a professional economist, a senior civil servant, and an academic leader. You honor him for his international role as a key architect of the CGIAR. Those of us who are compatriots value him for his many contributions during a time of optimism and rapid development in our country. His influence in Australia was enormous. Crawford was the first Director of the Research School of Pacific Studies at the newly formed Australian National University (ANU), an academic center that has played a considerable role in fostering both public policy and interactions in the South East Asian region. He then led the university as Vice Chancellor, and finally assumed the more ceremonial role of Chancellor. In all, he served the ANU for over 20 years. I never met him, though I was a member of the university at times when he was a senior figure. The work with Rolf Zinkernagel that was recognized by the 1996 Nobel Prize for Physiology or Medicine was done at the ANU, and was initiated during the time that Crawford was Vice Chancellor.

Quoting from a recent history[1] of the ANU, "he was short, unassuming in manner but vastly impressive for his depth of knowledge, understanding of issues and diplomatic skills". He is remembered in Australia as one of the seven dwarfs, a group of senior economists and civil servants of the 1950s and 1960s who shared the characteristic of being both extremely able and vertically challenged. Gabrielle Persley, who worked with Crawford, tells me that he never held a meeting until he knew what the outcome would be, and would gently steer the committee to the decision that he had made earlier. Crawford belonged to an era when public policy in the western democracies was more oriented to the common good, a time that many of us may look back to with a sense of nostalgia. I wonder what he would make of political agendas and economic strategies that emphasize personal greed as the most laudable of human characteristics.

All of us in this room are acutely aware of the importance of the CGIAR and are, I suspect, more than a little intimidated by the

problems that this organization is trying to address. There can be no doubt in the mind of anyone who has spent time in the developing world that the dismal predictions that Malthus made more than 170 years ago are rapidly coming to fruition. All the major Scientific Academies share this conclusion. Uncontrolled population growth is leading to increased social turmoil, degradation of the environment and the appalling prospect of periodic starvation at levels that will make current disasters seem like minor events[2]. This proceeds against a depressing backdrop of cultural and political agendas that do everything possible to deny the reality of what is happening and can function to diminish the meager resources currently available to address such issues. What is even more frightening is the sense that, as the pressures increase, the inevitable result will be a rise in reactionary politics and terrorism that will tend to make any rational response even more difficult. There will be no safe place. The CGIAR tries to deal with some of the consequences, though it is inherently unable to address the causes.

My association with the CGIAR stems from the six years (1986-1992) that I spent as Member, and latterly Chair of the Program Committee, of the Board of the International Laboratory for Research in Animal Diseases (ILRAD) in Nairobi, Kenya. As you know, ILRAD was combined with its sister field organization, International Livestock Centre for Africa (ILCA), some years back to constitute ILRI, the International Livestock Research Institute. Learning the acronyms is one of the first challenges for anyone who becomes involved in the international arena! It took me two years! The appointment as an ILRAD Board Member reflected my early training in veterinary science and a common interest in immunity to infection. The first nine years of my career were spent working in veterinary research institutes on diseases of domestic animals, while I switched some 27 years back to studying similar processes in laboratory mice and was thus transformed into a basic medical scientist. In my case, M.D. is "mouse doctor." The current reality is that all science is convergent, and the categories do not much matter.

The molecular genetic approaches that are used in biomedicine and animal and plant agriculture are essentially identical, with the latter activity benefiting from the massive basic biomedical research enterprise. You must forgive me for drawing examples as I talk from the animal side of things, but this is my area of expertise.

What does a laboratory rat like me have to say that could be of any value to international shakers and movers like you? The best that I can offer is that after 36 years in the game, I have some familiarity with the way that science operates. The mandate of the CGIAR is to seek solutions to the related problems of hunger, poverty and environmental degradation in the broadest sense through the application of science and technology. The scope of the activities and the magnitude of the problems are very clearly stated in the Report of the 3rd CGIAR System Review that is being presented at this meeting[2]. Economists, social scientists and facilitators in the Crawford tradition will obviously play enormously important roles. However, it is essential that both the funding agencies and the organization itself should also have the realities of science in perspective and understand something of the way that innovative scientists operate.

Make no mistake: if the CGIAR is to succeed in the mammoth task that it has undertaken, it is essential to promote environments which foster the mind jumps that provide novel solutions. A marvelous example of such innovation from the economics side is the Grameen Bank of Bangladesh, which was reviewed recently by Muhammad Yunus[3] for the readers of *Science,* a journal that publishes many of the cutting edge findings in laboratory-based research. I mention this because the fact that the Editors of *Science* are seeking such commentary reflects that many basic scientists are now taking a keen interest in real problems and their solutions. This move towards the practical is, I think, a direct consequence of the molecular biology/biotechnology revolution.

The first point that we must deal with as a research agency is that the level of government support for both national agricultural research programs and for the international scene is not high and is, in many cases, falling. Next year's annual budget for the US National Institutes of Health is expected to be in excess of $US 15 billion, representing a 14 percent increase over 1997-1998. The research budget for the USDA is about $1.5 billion, and for the whole of the CGIAR is less than $400 million. The American Howard Hughes Medical Institute spends in excess of $300 million, while the British Wellcome Foundation allocates £300 million to the biomedical area. My own institution, St. Jude Children's Research Hospital has an annual research budget in excess of $60 million for non-clinical, basic science. The US allocation for research on AIDS alone is approximately $1.5 billion, with 10 percent of that going towards the development of an AIDS vaccine.

Vaccination has been very much the focus of the international biomedical research community. Given the enormous difficulty of achieving widespread behavioral modification, it seems very obvious that the only way to deal with the increasingly disastrous AIDS pandemic in the poorer countries is to develop an effective and reasonably inexpensive vaccine. Those of us who work on viral immunity believe that such a product can be made, though there is currently no obvious strategy for success and the effort may take many years.

The Children's Vaccine Initiative (CVI), which was initiated in 1996, is seeking to give all the world's children the available childhood vaccines. Smallpox has been eliminated from the world 200 years after Edward Jenner introduced vaccination to the west. Fortunately, the lead-time from innovation to practical solution is now somewhat shorter. It looks likely that poliomyelitis will be gone by 2002 and the global eradication of measles now seems also to be a possibility. Paradoxically, the main threat to this initiative is in the industrialized world, where vocal minorities that have never seen these diseases are seeking to block all government mandated vaccination programs.

Anyone who is not frightened by the rise of the irrational in the so-called advanced countries should look up "Vaccination" on the Internet. The experience is almost as terrifying as listening to talk-back radio!

The CVI is being pursued as an exercise in compassion and common morality, involving a spectrum of organizations ranging from WHO to Rotary, which has paid for much of the vaccine. The underlying assumption for those who think in terms of stabilizing the global population is that people will act to reduce family size if there is a reasonable assurance that their children will survive. However, the issue is much more complex than that, as the move to have less children also requires the empowerment of women and other behavioral changes that are deeply threatening to elements that seem to have increasing force in some traditional cultures.

The CGIAR cannot, of course, afford to be drawn into controversies surrounding these broader social issues. The focus must be on strategies that involve the environmentally sensitive application of the science and technology of food production and supply[2]. Such issues are, in most instances, likely to be less emotive in the political sense. Battles concerning where and when the application of genetic engineering approaches will be applied to animal and plant agriculture are being fought out first in the donor countries of the industrialized world. A powerful force is the commercial interests that stand to make a profit. Those of us who have a broad profile are doing our best to ensure that public perceptions and legislation do not inhibit the sensible and careful application of the new technologies.

In particular, we need to convince those who are environmentally conscious of the possibilities for reducing the use of both chemical fertilizers and insecticides by the appropriate engineering of animals and plants. It is ironic that we are already injecting people with large doses of DNA in experimental viral vaccines made from human pathogens, while others are agonizing about the infinitesimal possibility that a disease

resistance gene that has been engineered into a plant will somehow enter human cells and cause cancer. Such gene transfer is not that easy. Most of us have been eating vegetables all our lives, but have not turned green and started to make chlorophyll! Scientists are increasingly aware that they cannot just squirrel away happily in their laboratories, but must also accept a broader responsibility to discuss, to educate and to dispel ill-founded myths and fears.

Some technologies that are very much in the CGIAR ballpark are ripe for application, particularly in the plant sciences. Problems where the solution seems obvious may be rapidly addressed by the direct application of established genetic engineering approaches. Such efforts are appropriate targets for short-term, directed funding mechanisms. Other problems are much more long-term and difficult.

The two cattle diseases that have been the consistent laboratory focus of ILRAD, and then ILRI, for more than 20 years are Trypanosomiasis and East Coast fever (ECF). Biologically, Trypanosomiasis is at least as complex and difficult to deal with as human AIDS. The cause of ECF is a protozoan parasite, *Theileria parva*, that has a life cycle in many senses comparable to that of the *Plasmodium* species responsible for human malaria. The difference is that *T. parva* grows in the lymphocytes, or white blood cells, while *Plasmodium* is in the erythroid, or red cell lineage. Candidate vaccines for both these diseases are at roughly equivalent stages of development, though the dollars spent on *Theileria* research must be 10 percent of those available for malaria. The CGIAR does get value for money! The medical community accepts that malaria is an enormously difficult problem. One of the reasons that I work in medical research is that there has been a tendency to assume that veterinary diseases can be dealt with by quick, simple and naive approaches, a perception that is patently absurd.

The point is that research on a disease as complex as ECF needs to be open and imaginative, looking for novel insights and

exploring different avenues. This is why it is so important that a substantial component of the budget for each of the CGIAR Centers should be flexible and available for the pursuit of long-term goals, with quality control depending on regular, scientific review. Holding scientists to an exclusive focus on immediate, practical outcomes ensures mediocrity and the rapid defection of talented investigators. If the American research enterprise over the past 50 years had followed "short term solution" models we would still be paying engineers to build better iron lungs and cannon builders to put a man on the moon. Innovative science is a great deal more than engineering, whether it be mechanical, electrical or genetic, though there is always a stage where the engineers and managers take over to see the product through to production and distribution.

Both ECF and Trypanosomiasis can be used to illustrate another point that concerns anyone who looks at the international agricultural research enterprise. The question is: "Should the CGIAR Centers in the developing world focus only on end-stage, practical objectives, while the more imaginative and innovative work is left to Universities and Research Institutes in the industrialized countries?" I know science and I know scientists, and have absolutely no problem in telling you that this would be a fatal mistake.

The primary requirement for any viable research enterprise is that the scientific staff must be of top quality. First rate scientists will tolerate many minor annoyances, but they will not accept a situation where it is impossible to explore and to test ideas. The best young investigators will take on the challenge of studying a complex disease problem like Trypanosomiasis, but they will not tolerate a short leash and being told what to do. Put such people back in an academic environment where they do not see cattle with Trypanosomiasis and there is a real risk that they will lose focus and go of on some intellectually satisfying, but less practically-oriented direction. Such research is readily funded by biomedical research grants, and it is easy to forget quickly about the tough and in some senses unglamorous

problems that are being tackled by the CGIAR. There is no Nobel Prize for agriculture!

The costs and regulatory constraints on maintaining large domestic animals infected with exotic diseases like Trypanosomiasis or ECF in Europe or North America are now prohibitive. Such studies must be done in the countries where the problem exists. Some aspects of ECF immunity can, for example, be analyzed by putting lymphocytes on a plane in Nairobi and sending them to Utrecht or to Miami. However there is a great deal of work that needs to be done either close to the experimental animal, or directly in the field. A prime example is the marker/segregation analysis aimed at finding genes conferring resistance to Trypanosomiasis that has been in progress for some years at ILRI. Identification of these genes could lead to their rapid dissemination through the African herd, either by more traditional methods such as artificial insemination or by advanced genetic engineering approaches. Such large-scale cattle breeding experiments that require challenge with the infecting organism are only possible in Africa.

Having said this, there is a good case for encouraging the development of funding mechanisms that facilitate research enterprises based both in a major European or American university and in a CGIAR Center. The exchange of scientists, particularly at more junior levels, and the ready access to the extensive technological resources that exist only in the industrialized countries has the potential to move programs along much more effectively. There is also the likelihood of multiplier effects, as scientists discussing their work in an open academic environment interest others in the problem. Living for even a few months in a developing country is also a great experience for young scientists, and increases the national pool of talented and knowledgeable people that can be drawn on later to assist in formulating and applying AID agendas and the like. I benefited enormously from the time I spent on the ILRAD Board and learned a great deal, especially, from my African colleagues. It was a civilizing experience for me.

A further major, though somewhat understated, role of the CGIAR Centers is that they provide a focus for training local scientists. The value of such experience can be greatly enhanced if some time is also spent in an affiliated institution in the Northern Hemisphere. Modern molecular biology does not need enormously sophisticated laboratories and is, in fact, being pursued very effectively in a number of countries that none of us would think of as being at the forefront of science. It is important to have sophisticated, in-country expertise at the level of, for example, the National Agricultural Research Services, both to pursue scientific applications and to provide sound advice to governments. If the ILRAD/ILCA/ILRI example is typical, the CGIAR has been doing an excellent job in this regard. We calculated earlier this year that this small (by biomedical research standards) operation has trained over 300 young scientists, including 55 from Ethiopia and 70 from Kenya. There are currently 55 graduate students at ILRI.

I have tried to use this lecture to convey some sense of the realities of the scientific culture. Progress in any scientific endeavor will only be as good as the people involved. It is sometimes difficult for those who work in oligarchies to understand that first class research investigators do not think like civil servants, will not be micro-managed, and are not inter-changeable, disposable products. Their ultimate realities are the difficult scientific problems that they are addressing, not the perceptions of a senior administrator or a political master. Active scientists can often be a pain in the neck for administrators!

There is nothing that competitive scientists loathe more than bureaucratic structures, filling in forms and the perception that managers are proliferating at the expense of the research programs. This needs to be understood if the CGIAR is to retain and to continue recruiting those with real ability, both as scientific investigators within the various Centers and as collaborators at major institutions in the industrialized world. The latter type of person is generally well funded, and tends to

have little time for either administrative trivia or for unrealistic expectations of "quick-fix" solutions. Though there are many people with scientific credentials, the pool of outstanding people is very limited.

The almost exponential growth of the biomedical research enterprise in the USA means that the competition for talent is enormous. Modern molecular medicine is already absorbing skilled people with basic training in the molecular biology aspects of animal and plant agriculture. I have several young colleagues at St. Jude Hospital who did their doctoral studies in the plant sciences or in veterinary medicine, but have switched to basic cancer research and cell biology.

The optimal way for donors to promote a situation where there can continue to be real innovation within the CGIAR structure is to provide a good measure of funding to support the type of sustained effort that is likely to lead to long-term solutions. The review of the science and the progress towards stated goals is best left to the excellent mechanisms that the CGIAR has in place. Providing answers to the linked problems of poverty and hunger[2] requires that the Centers should not be forced to focus most of their efforts on readily achieved, but inherently limited, short-term goals. Flexibility and freedom of action are fundamental to achieving rapid scientific progress.

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ABOUT THE SPEAKER

Dr. Peter Doherty is an Australian immunologist who currently serves as chairman of the Immunology Department at St. Jude Children's Research Hospital in Memphis, Tennessee. His long and distinguished career includes appointments at leading medical research institutions in Australia and in the United States. From 1986 to 1992, Dr. Doherty served as a member of the Board of Trustees of the CGIAR International Laboratory for Research in Animal Diseases (ILRAD) in Nairobi, Kenya.

Dr. Doherty, together with his colleague Dr. Rolf Zinkernagel, received the Nobel Prize for Medicine in 1996 for ground-breaking research to discover precisely how the human immune system recognizes virus-infected cells and targets them for destruction. Those discoveries have led to a new understanding of organ rejection after transplants, a better comprehension of genetic susceptibility to disease, and new approaches for vaccines.